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ning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR THE TREATMENT OF DEMENTIA BASED ON APO E GENOTYPE

(57) Abstract: This invention relates to methods to prevent worsening of and/or to improve cognitive functioning and behaviour problems in patients with dementia by means of ApoE genotyping to guide the use of AChEI drugs, including rivastigmine. Also included are kits for determining ApoE4 status and recommended treatment strategy.

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A. CLASSIFICATION OF SUBJECT MATTER
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B. FIELDS SEARCHED

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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MEDLINE, BIOSIS, EMBASE, CHEM ABS Data, WPI Data, EPO-Internal, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WINBLAD B ET AL: "A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD" NEUROLOGY, vol. 57, no. 3, 14 August 2001 (2001-08-14), pages 489-495, XP009023203 ISSN: 0028-3878 page 493, right-hand column, paragraph 3 --- -/--	1,2,5-9, 12-14, 17-20, 23,24

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FARLOW MARTIN R ET AL: "Apolipoprotein E genotype and gender influence response to tacrine therapy" ANNALS OF THE NEW YORK ACADEMY OF SCIENCES; APOLIPOPROTEIN E, 1996, pages 101-110, XP009023190 Conference; Chicago, Illinois, USA; October 21-22, 1995, 1996 New York Academy of Sciences {a}, 2 East 63rd Street, New York, New York 10021, USA Series: Annals of the New York Academy of Sciences (ISSN 0077-8923) page 104, paragraph 3	1,2,5-9, 12-14, 17-20, 23,24
X	SJOGREN M ET AL: "Tacrine and rate of progression in Alzheimer's disease: Relation to ApoE allele genotype" JOURNAL OF NEURAL TRANSMISSION, vol. 108, no. 4, 2001, pages 451-458, XP002265850 ISSN: 0300-9564 abstract	1,2,5-9, 12-14, 17-20, 23,24
X	AERSSSENS J ET AL: "APOE genotype: no influence on galantamine treatment efficacy nor on rate of decline in Alzheimer's disease." DEMENTIA AND GERIATRIC COGNITIVE DISORDERS. SWITZERLAND 2001 MAR-APR, vol. 12, no. 2, March 2001 (2001-03), pages 69-77, XP009023193 ISSN: 1420-8008 abstract	1,2,5-9, 12-14, 17-20, 23,24
X	NOBILI FLAVIO ET AL: "Brain perfusion follow-up in Alzheimer's patients during treatment with acetylcholinesterase inhibitors" JOURNAL OF NUCLEAR MEDICINE, vol. 43, no. 8, August 2002 (2002-08), pages 983-990, XP001156838 ISSN: 0161-5505 abstract	1-24
X	WO 95 16791 A (UNIV MCGILL ; POIRIER JUDES (CA)) 22 June 1995 (1995-06-22) the whole document	33-42
X	US 6 391 553 B1 (AMOUYEL PHILIPPE ET AL) 21 May 2002 (2002-05-21) column 3, paragraph 5 column 4, paragraphs 2,3	33-39, 41,42

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INTERNATIONAL SEARCH REPORT

Int. Application No
PCT/EP 03/08719

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Derwent Publications Ltd., London, GB; AN 2000-264443 XP002265851 "Apolipoprotein E4-specific monoclonal antibody used for immunoassay of APoE does not react with ApoE isoforms 2 and 3" & JP 2000 069963 A (IGAKU SEIBUTSUGAKU KENKYUSHO:KK), 7 March 2000 (2000-03-07) abstract</p>	40
P,X	<p>STEFANOVA E ET AL: "Cerebral glucose metabolism, cerebrospinal fluid-beta-amyloid1-42 (CSF-Abeta42), tau and apolipoprotein E genotype in long-term rivastigmine and tacrine treated Alzheimer disease (AD) patients." NEUROSCIENCE LETTERS. IRELAND 27 FEB 2003, vol. 338, no. 2, 27 February 2003 (2003-02-27), pages 159-163, XP001156837 ISSN: 0304-3940 the whole document</p>	1-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/08719

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9516791	A	22-06-1995	CA 2111503 A1	16-06-1995
			AU 1189395 A	03-07-1995
			WO 9516791 A1	22-06-1995
US 6391553	B1	21-05-2002	FR 2765591 A1	08-01-1999
			AU 8346498 A	25-01-1999
			EP 0983391 A1	08-03-2000
			WO 9901574 A1	14-01-1999
			JP 2002510975 T	09-04-2002
JP 2000069963	A	07-03-2000	NONE	